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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,141	ANDERSON ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5,16-28,30 and 33-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,16-28,30 and 33-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S10.0

DETAILED ACTION

1. Applicant's amendment, filed 7/8/05, has been entered.

Claims 29 and 31 have been canceled. Claims 1, 4, 6-15 and 32 have been canceled previously.

Claims 2, 3, 30, 32, 33 and 34 have been amended.

Claims 2, 3, 5, 16-28, 30, and 33-39 are pending.

Applicant's election with traverse of multiple sclerosis (Group II-C) as the disease species has been acknowledged.

Claims 2, 3, 5, 16-28, 30 and 33-39 as they read on treating multiple sclerosis with anti-gp39 antibodies are under consideration as the elected invention.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's amendment, filed 7/8/05, which appears to reiterate applicant's previously amendment, filed 4/12/05.
The rejections of record can be found in the previous Office Action.

3. Upon a review of the instant specification, it does not appear that applicant has provided the appropriate SEQ ID NOS. disclosed in the specification, as required for applications that contain sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825.

Applicant is required to amend the specification to indicate the appropriate SEQ ID NOS. in accordance with 37 CFR 1.821-1.825, particularly 37 CFR 1.821(d).

Applicant is required to fulfill these requirements.

4. Applicant's amended claims, filed 7/8/05, have obviated the previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "substantially non-agonistic of a T cells activation response(s)".

5. Applicant's provision of the Cawley Declaration has provided the appropriate assurances for the 24-31 antibody that obviates the previous rejection under 35 U.S.C. 112, first paragraph, enablement for the deposit of biological materials.

However, amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

6. Applicant's amended claims, filed 7/8/05 has obviated the previous rejections under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 2, 3, 5, 16-28, 30 and 33-39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Black et al. (U.S. Patent No. 6,001,358) in view of the art known methods to screen for inhibitors of cytokines and proliferation in view of Schrader et al. (U.S. Patent No. 5,627,052), Burkly et al. (US2002/0028202 A1) and Wilson et al. (U.S. Patent No. 6,372,208 B1) essentially for the reasons of record.

Applicant's arguments, filed 7/8/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that Black et al. does not describe or suggest a method of obtaining anti-gp39 antibodies that includes steps of assaying for and identifying non-agonistic antibodies with the characteristics of human T cell activation.

While applicant relies upon the teachings of Blair et al. (J. Exp. Med. 191: 651- 660, 2000) and Blotta et al. (J. Immunol. 156: 3133-3140. 1996) to indicate the agonistic properties of anti-gp39 antibodies on T cells,

However these references appear to rely upon the cross-linking of anti-gp39 antibodies to achieve such agonistic properties.

While applicant has also relied upon the data in Table 5 of Black and the possible distinctions between anti-mouse gp39 antibodies versus anti-human gp39 antibodies to support the unobviousness of the prior art rejection,

it has been pointed out that both Black et al. and Wilson et al. teach inhibitory anti-CD40 ligand (anti-gp39) antibodies and their effects on T cell mediated activation and functions and that Wilson et al. makes no distinction between inhibitory anti-mouse gp39 antibodies versus anti-human gp39 antibodies.

The following is reiterated for applicant's convenience.

Black et al. teach methods of treating disease condition wherein gp39 inhibition is therapeutically beneficial (columns 13-14 and 31-34), including multiple sclerosis with column 14, line 40 and column 32, line 67) with antibodies that bind gp39 (CD40 ligand), which block signals delivered via CD40 (See Examples 2, 3 columns 22-23; Examples 11-17 on columns 28-38 (see entire document).

In addition, Black et al. teach chimeric, humanized, and primatized antibodies, including the use of different heavy chain constant regions (IgG1, IgG3, IgG4), with conservative amino acid substitutions such as Kabat positions 229 and 236 as well as the 24-31 antibody specificity and its variable regions amino acid sequences encompassed by the claimed methods (see entire document, including Background of the Invention, including columns 6-7; Summary of the Invention; Detailed Description of the Invention, including columns 13-22; Claims). Further, it is noted that Black et al. teach that it was known that $gp39^{+}$ T cells produced IL-2, IL-4 and γ-interferon (see column 4, paragraph 1). In addition, Black et al. teach modes of

administration and dosages of antagonistic anti-gp39 antibodies encompassed by the claimed methods (see columns 33-38).

Black et al. differs from the claimed methods by not disclosing the art known use of screening for inhibitors of cytokine activity such as IL-2, IL-4 and ϒ-interferon as well as cell proliferation per se in selecting antagonistic anti-gp39 antibodies.

Schrader et al. teach methods of producing antibodies of a desired function to a variety of antigens, including IL-2 and ϒ-interferon, including the section of antibodies that neutralizes a growth factor or detection of antibodies that neutralize IL-2 (e.g. see columns 8-9, overlapping paragraph) and exemplifies the detection of antibodies that neutralize IL-2 (see Example 1 on columns 21-22) (see entire document, including Summary of the Invention and Detailed Description of the Invention).

Burkly et al. teach known methods of assaying or screening the ability of antagonists such as antibodies to block a response to a particular cytokine (e.g. IL-2) (See GC Chain Blocking Agents and Production of GC Blocking Antibodies on pages 7-8 and Testing Compounds of the Invention for Biological Utility on page 13). Burkly et al. note that it will be recognized by one skilled in the art, that these screens can be arranged to discover antibodies whose activities are conspicuous in one or more of these assays (see paragraph 095 on page 8) and that one of skill in art may easily determined using well known methods whether a particular blocking agent displays biological activity (see Testing Compounds of the Invention for Biological Utility on page 13).

Wilson et al. teach that CD40 ligand – CD40 interactions are desirable given its broad activity in both T helper cell activation and function as well as the absence of redundancy in its signaling pathway (see entire document, particularly column 6, paragraphs 4-5). In addition, Example 8 describes analyzing the effect of CD40 ligand blockade with antibodies on T cell activation using both in vitro and in vivo assays, including T cell proliferation (see columns 20-22).

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Schrader et al., Burkly et al. and Wilson et al. to those of Black et al. to screen and obtain antagonistic anti-gp39 antibodies with the ability to inhibit cytokines produced by activated T cells, including the inhibition of IL-2, IL-4 and γ-interferon, which were known to be products of the T cells targeted by antagonistic anti-gp39 antibodies. According to Black et al., a person of ordinary skill in the art would have been motivated to produce this resultant ability of anti-gp39 antibodies to inhibit cytokine activity by activated T cells in order to test and select for those anti-gp39 antibodies that had the described properties of inhibiting gp39:CD40 interaction and the resultant ability of such antibodies to inhibit T cell mediated activation of immune response in the treatment of various conditions and disorders, including multiple sclerosis. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

As indicated previously, once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case the teachings of the secondary references provide clear teachings of the known assays to test inhibitory antibodies, including antibodies that inhibit T cell activation and proliferation, including antibodies that inhibit CD40 ligand : CD40 interactions.

Both Black et al. and Wilson et al. teach inhibitory anti-CD40 ligand (anti-gp39) antibodies and their effects on T cell mediated activation and functions.

Given the role of various cytokines such as IL-2, IL-4 and γ-interferon, which were known to be products of the T cells targeted by antagonistic anti-gp39 antibodies, play in immune responses, one of ordinary skill in the art would have been motivated to screen and test for the properties of antagonistic anti-CD40 ligand antibodies that inhibited T cell activation and proliferation in the selection of such inhibitory antibodies that can regulate the various manifestations of T cell activation and function.

The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144

Applicant's arguments are not persuasive.

8. No claim allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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September 12, 2005